

What is claimed is:

1. A transgenic mouse, the genome of the cells of which stably comprise a DNA molecule which comprises a human genomic DNA sequence comprising a human tau promoter and which DNA sequence encodes human tau, wherein the DNA sequence is expressed in the transgenic mouse so as to result in the transgenic mouse expressing six isoforms of human tau, wherein the transgenic mouse does not express endogenous murine tau, wherein the DNA sequence comprises one SrfI restriction site in the human tau coding region, and wherein the transgenic mouse accumulates filamentous tau in dendrites of hippocampal neurons.
2. The transgenic mouse of claim 1 which develops abnormal spinal cord pathology.
3. The transgenic mouse of claim 1 which has motor abnormalities.
4. The transgenic mouse of claim 1 wherein the human genomic DNA sequence comprises at least one alteration.
5. The transgenic mouse of claim 4 wherein the alteration comprises at least one mutation.
6. The transgenic mouse of claim 4 wherein the alteration comprises at least one insertion or at least one deletion.
7. The transgenic mouse of claim 1 which has a dementing disorder or a neurodegenerative disorder.
8. The transgenic mouse of claim 1 which accumulates abnormal tau in the cell bodies and dendrites of neurons in the hippocampus, neocortex or brainstem.

9. The transgenic mouse of claim 1 wherein at least one human tau isoform has an abnormal conformation.
10. A transgenic mouse, the genome of the cells of which stably comprise a DNA molecule which comprises a human genomic DNA sequence comprising a human tau promoter and which DNA sequence encodes human tau, wherein the DNA sequence is expressed in the transgenic mouse so as to result in the transgenic mouse expressing six isoforms of human tau, wherein the DNA sequence comprises one SrfI restriction site in the human tau coding region, and wherein the ratio of the six isoforms is altered in the transgenic mouse relative to the ratio in humans.
11. Progeny of the transgenic mouse of claim 1 or 10.
12. A method for expression of human tau in a mouse, comprising preparing the transgenic mouse of claim 1 or 10.
13. The method of claim 12 wherein the human genomic DNA sequence comprises at least one alteration.
14. The method of claim 12 wherein the alteration comprises at least one insertion or at least one deletion.
15. The method of claim 12 wherein the alteration is associated with a dementing disorder.
16. The method of claim 12 wherein the alteration is associated a neurodegenerative disorder.

17. The method of claim 12 wherein the human tau isoform has an abnormal conformation.
18. A method of using a transgenic mouse which expresses human tau to screen for an agent that reduces or inhibits a neurodegenerative disorder, comprising:
  - (a) administering the agent to the transgenic mouse of claim 1; and
  - (b) determining whether the agent reduces or inhibits a neurodegenerative disorder in the transgenic mouse relative to a transgenic mouse of claim 1 which has not been administered the agent.
19. A method to screen for an agent that reduces or inhibits abnormal tau formation, comprising:
  - (a) administering the agent to an organotypic slice culture comprising cells obtained from the brain of the transgenic mouse of claim 1; and
  - (b) determining whether the agent reduces or inhibits abnormal tau formation in the organotypic slice culture relative to an organotypic slice culture which has not been administered the agent or a corresponding organotypic slice culture comprising cells obtained from the brain of the transgenic mouse of claim 10.